

**Pricing and Reimbursement Challenges for Fixed Dose Combination  
Cardiovascular Drugs and Intravenous Oncologies**

by

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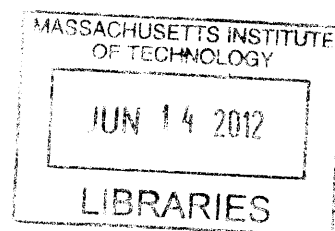
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# **Pricing and Reimbursement Challenges for Fixed Dose Combination Cardiovascular Drugs and Intravenous Oncologics**

By

Drew Cronin-Fine

Submitted to the Harvard-MIT Division of Health Sciences and Technology on May 21, 2012 in Partial Fulfillment for the Degree of Master of Science in Health Sciences and Technology at the Massachusetts Institute of Technology

## **Abstract**

Over the past ten years there has been increasing public concern regarding the rising costs of pharmaceuticals. Drug expenditure is the fastest growing sector of healthcare costs in the United States. The structure of the U.S. healthcare system allows pharmaceutical companies to freely price their drugs. Then payers decide whether and how to cover these drugs. Payers have at their disposal several utilization management tools, such as tiering and prior authorizations, to steer their members to less costly drugs. However, the ability of payers to implement these tools varies significantly depending on whether the drug is covered under the pharmaceutical benefit / Medicare Part D provisions of healthcare plans or the medical benefit / Medicare Part B provisions. Drugs covered under the pharmaceutical benefit / Part D are distributed via retail pharmacies and, in general, are oral pills. Drugs covered under the medical benefit / Part B are physician administered drugs and, in general, are injectables or intravenous drugs.

As pharmaceutical companies increasingly price their drugs at higher and higher levels, payers must take a drug's pricing into account when determining how to cover these drugs. This thesis assesses the role pricing plays in how a drug is covered. Two different classes of drugs were chosen to examine this topic: fixed dose combination (FDC) cardiovascular drugs and intravenous oncologics. FDC cardiovascular drugs were chosen because they are covered under the pharmacy benefit / Part D and are considered to have questionable efficacious value over their individual drug components. Intravenous oncologics were chosen because they are covered

under the medical benefit / Part B and represent a highly politicized therapy area. These two therapy areas are illustrative of strongly contrasting classes of drugs.

Literature review and public sources were used to obtain prices for the select cardiovascular FDCs and oncologics. Medicare's Formulary Finder was used to obtain the coverage level for the cardiovascular FDCs. This preliminary information showed that the most expensive of the select FDCs, Caduet, has the worst coverage. The literature review suggested that Provenge and Avastin, the most expensive of the select oncologics, had difficulty obtaining coverage. To confirm these results, interviews were conducted with a variety of payers. These interviews focused on what factors went into the coverage decision-making process for cardiovascular FDCs and intravenous oncologics. Interviews were also conducted with an oncologic distributor to determine distributors' impact on price.

We hypothesized that price was the driving reason for Caduet's, Provenge's, and Avastin's relatively poor coverage. However, our hypothesis was not entirely confirmed. Payers confirmed that price and contracting were the driving factors for Caduet's relatively poor coverage, but they indicated that the situation was not as simple for the intravenous oncologics. Although price does play a small role in the coverage decision-making process for intravenous oncologics, other factors such as public policies and the unmet need in the therapy area drive coverage decisions more than price. Additionally, payers indicated that they lack the ability to steer members to less costly intravenous oncologics due to the drug acquisition and reimbursement structure of the medical benefit. Consequently, payers are beginning to utilize new techniques such as specialty pharmacies to help control utilization of these products. Also, other organizations such as certain oncologic distributors are attempting to implement cost-effective guidelines for intravenous oncologics. Our results have significant implications for what pharmaceutical companies should be considering when pricing their drugs, and highlight the pricing and coverage issues in the current healthcare system's structure that payers and other organizations are facing.

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## **Dedication**

*To my parents, Lynn and Howard, for their never ending support in whatever endeavors I choose to pursue.*

*To my brother, Lee, for always standing by me and being there with inappropriately timed jokes.*

*To my advisors and mentors at Harvard and MIT, who have given me their time and support to help me achieve my goals.*

## Acknowledgements

I have always been drawn to the healthcare field. The area is unique in that healthcare decisions often result in life or death. As a corollary, I am intrigued by how the business world has come to analyze and place a quantitative value on life. This is what led me to my thesis topic. In the U.S. healthcare system, pharmaceutical companies decide at what level to price their drugs, and then payers determine whether and how to cover the drug at that list price. Thus, payers play the role of checking a pharmaceutical company's ability to price its drugs unreasonably high. However, certain therapy areas such as oncology are hard to apply reason to. I chose this thesis topic to explore how payers and our healthcare system place limits and value on a drug which may have the potential to save a person's life.

My sincerest appreciation and gratitude go to my thesis advisors, Professor Teo Dagi and Professor Regina Herzlinger, for their constant support and guidance throughout my thesis process. Their help in focusing my thesis topic and directing my research has been essential. Additionally, I would like to thank all of the payers and distributors who took the time to speak with me, as well as the other experts who helped me narrow my thesis topic.

The Biomedical Enterprise Program is a unique and valuable program for anyone who desires to enter the healthcare field. The combination of healthcare specific business classes, medical school classes, and classes which bring you into hospitals to observe patient treatment has caused my knowledge of healthcare to grow tremendously in the past few years. The community of biotech entrepreneurs, physicians, and healthcare investors that BEP brings together is exceptional. I am honored to have been a part of it.

Finally, I would like to thank my fellow BEP classmates for the dinner parties, the academic support—especially in pathology—and for simply always being there when I needed help. I truly enjoyed getting to know everyone, and look forward to remaining friends for years to come.

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## Chapter 1: Introduction

The increasingly high prices of pharmaceuticals have generated significant public criticism in recent years. When Dendreon introduced its prostate cancer drug Provenge with a \$93,000 price tag, Centers for Medicare & Medicaid Services (CMS) initiated a national coverage review just two months after the drug's launch. Genentech established a \$55,000 price cap on its drug Avastin after the public outcry over its \$100,000 annual cost for non-small cell lung cancer patients.

Typically, the health insurance companies, i.e., the primary payers in the employment-based healthcare system in the U.S., are the ones who reign in these prices. In their attempts to control drug costs, these payers have developed several techniques over the years to direct member drug utilization to the least expensive options. However, there are significant differences in how payers are able to manage drugs dispensed by a retail pharmacy versus drugs administered by physicians and/or nurses in an outpatient setting. These differences allow payers to have greater management control over drugs administered at the retail pharmacy level.

Payers' drug utilization management techniques are continuing to evolve and include tiered formularies, step edits, prior authorizations, and quantity limits. These techniques have received academic attention and exploration, but little seems to be known about what factors go into a payer's management decision-making process when evaluating a new drug. Are decisions based primarily on efficacy? How much of a role does the price of a drug play in the process? How does this differ by class of products? To explore these issues further, we chose a set of drugs from two therapy areas to examine why payers made the decisions they made in terms of covering and managing these drugs.

The first class of drugs chosen was fixed dosed combination drugs (FDCs) indicated for the prevention of cardiovascular disease, specifically Caduet, Vytorin, and Exforge. All of these drugs are a combination of two drugs currently on the market, one of which is generic. They are distributed via retail pharmacies and have questionable added value considering their

components are already commercially available. Thus, we believe they are an ideal class of drugs for payers to strongly manage for cost control purposes.

In contrast, the second class of drugs we chose is more difficult to manage. The second class of drugs chosen was intravenous oncology drugs (IV oncologics), specifically Provenge, Avastin, Erbitux, and Vectibix. These drugs are all administered at either physicians' offices or infusion centers via 60-to-90 minute infusions, and are normally covered under the medical benefit provisions of healthcare plans. The prices of these drugs tend to be relatively high compared to FDCs and other drugs. However, since oncology is a very political therapy area, we believe payers would have to balance many factors when deciding how to manage these drugs.

Although the FDC Caduet and the IV oncologics Provenge and Avastin are FDA approved and considered beneficial to patients, they have higher prices than the other drugs in their classes. Based on this observation, we hypothesized that the relatively high list prices of Caduet, Provenge, and Avastin would result in greater access restrictions, and that price is the driving factor that has caused payers to provide relatively restricted coverage.

The primary purpose of this thesis is to examine the relative level of importance of different factors considered by payers in their decision-making processes for managing these two classes of drugs. Specifically, we examine the varying role of price in the reimbursement process. Further, we explore the different utilization management techniques for drugs covered under the pharmacy benefit and the medical benefit provisions of healthcare plans.

This thesis is organized in the following manner. We begin with a brief summary of the origins of the employment-based healthcare system and Medicare system in the U.S., followed by a discussion of how drugs are covered under the medical benefit / Part B and the pharmacy benefit / Part D of health plans. Next we examine the evolution of utilization management tools used by payers to direct patients to less expensive therapies and prevent overutilization. Then we discuss the general coverage decision-making process that payers use to evaluate new drugs, as well as physicians' incentives in prescribing certain types of drugs. We then give some background on the controversy surrounding the relatively high price of IV oncologics and a brief discussion of

the coverage rationale for fixed dose combination drugs. With this knowledge base, we discuss in detail the methods used for evaluating the hypothesis, including a literature review of the pricing and reimbursement of the selected IV oncologics and FDCs. Then we lay out a comprehensive analysis of results followed by a discussion of their implications regarding the increasing prices of drugs and the role payers can play in controlling the escalating prices. We follow this with a discussion of the strategies payers and pharmaceutical companies may want to consider employing in managing IV oncologics and FDCs. Finally, we describe possible follow-up studies and conclude with a summary of the analysis and implications.

## Chapter 2: Background

### *Pharmaceutical Reimbursement in the U.S.*

America's employer-provided health insurance system evolved and expanded primarily as a result of domestic wage controls during World War II. Due to the 1942 Stabilization Act, employers were highly limited in their ability to increase their employees' wages.<sup>27</sup> However, the Stabilization Act passed by Congress did not apply to fringe benefits. Thus, in lieu of increasing employees' wages, many employers began to offer health insurance. The trend towards employer-provided health insurance was then further strengthened when Congress declared in 1954 that employer contributions and premiums for employee health insurance would be treated as tax-deductible business expenses and, for the employee, these contributions and premiums would not be considered taxable compensation.<sup>4, 27</sup>

A major milestone in U.S. health insurance policy occurred in 1965 with the implementation of Medicare, a program that provides health insurance to American citizens over the age of 65 years. Medicare was then expanded in the 1970s to include individuals under the age of 65 years with permanent disabilities, such as end-stage renal disease. In 2003, Congress enhanced Medicare even further when it passed the Medicare Modernization Act which provided Medicare participants with prescription drug coverage for the first time, starting in 2006.<sup>3</sup>

Today, Medicare is composed of four parts: Part A – hospital insurance, Part B – medical insurance, Part C – Medicare Advantage Plans (e.g., HMOs), and Part D – prescription drug benefits. More specifically, Medicare Part D provides coverage only for prescription drugs, i.e. drugs that are dispensed at a pharmacy rather than at a physician's office or at a hospital. Drugs administered at hospitals are covered under Part A via bundled payments in which Medicare pays hospitals based on a patient's condition rather than for the specific items used for treatment. Medicare Part B covers, among other items, drugs administered at a physician's office, such as chemotherapy for cancer patients administered at a doctor's office, freestanding clinic, or hospital outpatient setting.<sup>10</sup> Medicare Advantage Plans are fixed-fee plans, as opposed to fee-for-service plans, and prescription drugs under these plans are generally covered under Part D.

Commercial insurance plans generally cover drugs in a manner similar to Medicare. That is, the medical benefit provisions of commercial plans usually cover drugs administered on an inpatient basis or at a physician's office, freestanding clinic, or hospital outpatient setting. Separate pharmacy benefit provisions cover drugs distributed via retail pharmacies, similar to the way Medicare Part D operates.

### ***Drug Utilization Management***

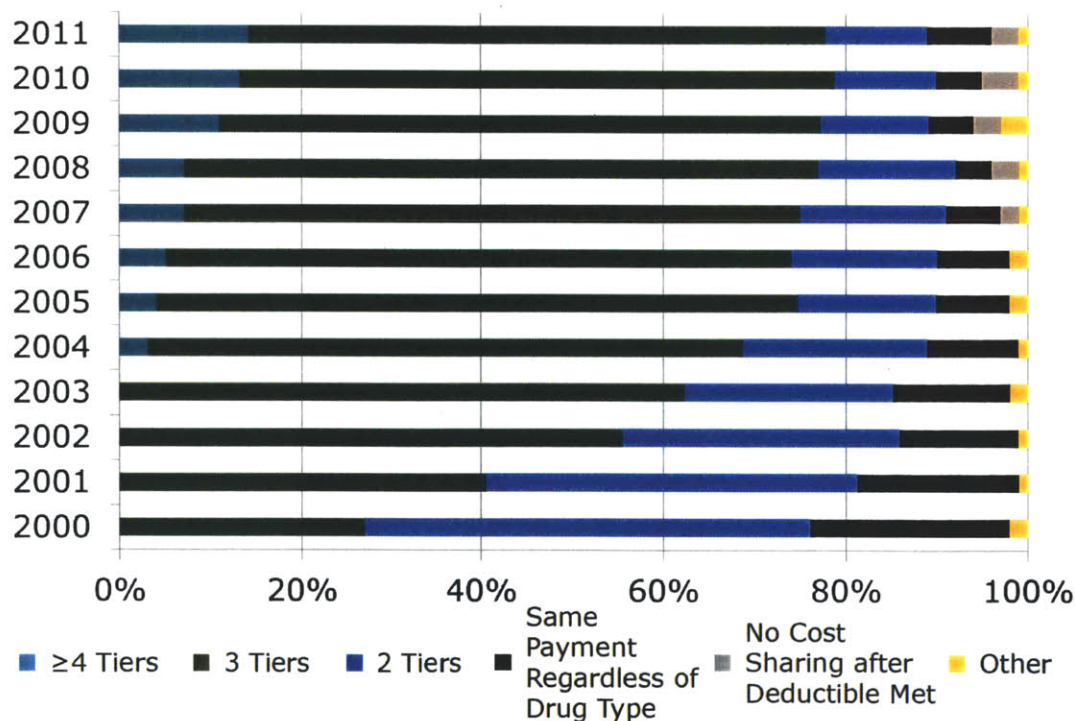
Rising prescription drug spending has been a concern for payers for many years. Cost escalation in the 1990s and 2000s was particularly rapid. For example, drug spending increased by 14.3% from 2000 to 2002 and 10.2% in 2003.<sup>2</sup> As a result, payers began to employ more aggressive tactics to curtail overutilization of pharmaceuticals and, in some instances, to direct members towards using the least expensive drug in a category.

In the 1990s, a new approach known as tiered formularies was developed for managing rising prescription drug spending and is highly prevalent today. Two-tier plans generally have one tier for generic drugs (Tier 1) and one tier for brand-drugs (Tier 2), i.e. drugs that are still covered by a patent. The generic tier has a lower copayment than the brand-drug tier. Thus, members are financially incentivized to use generic drugs, which tend to cost significantly less for the payer than brand-drugs. Three-tier formularies have a generic tier (Tier 1), a preferred brand-drugs tier (Tier 2), and a non-preferred brand-drugs tier (Tier 3). Preferred drugs are generally brand-drugs with a lower cost to the payer, obtained either through a lower list price or through contracting with pharmaceutical companies for a lower price. However, some drugs are covered under Tier 2 due to other reasons such as the severity of the disease state or lack of alternative treatments. The list of preferred brand-drugs differs by payer. Copayments for three-tier plans increase according to tier. Thus, payers are attempting to incentivize members to first use generic drugs, then preferred brand-drugs. Four-tier plans are similar to three-tier plans in that they have a generic tier, preferred brand-drugs tier, and non-preferred brand-drugs tier. However, they also have a tier (Tier 4) generally for high-cost biologics and life style drugs.

A rapid increase in the implementation of three- and four-tier formularies occurred between 2000 and 2011 (see Figure 1). One- and two-tier plans occupied 71% of the market in 2000, but only occupied 18% of the market in 2011. In 2000, there were no four-tier plans and only 27% of the market was three-tier plans. By 2011, four- and three-tier plans occupied 14% and 63% of the market, respectively.<sup>1</sup> A study showed that Medicare beneficiaries in three-tier plans had 14.3% lower total drug expenditure compared with individuals in lower tiered plans.<sup>14</sup> Nevertheless, spending on prescription drugs has continued to outpace inflation, increasing at an average annual rate of 4.625% from 2007 to 2010.<sup>5</sup>

### Figure 1: Distribution of Covered Workers Cost-Sharing Formulas for Prescription Drugs

Source: Kaiser Family Foundation. Employer Benefits Survey, 2011



Over the last decade, payers have increased the copayments for every tier in an attempt to curtail unnecessary prescription drug utilization. The average copayments for Tiers 1, 2, and 3 in 2000 were \$8, \$15, and \$29, respectively. The average copayments for Tiers 1, 2, and 3 in 2011 were \$10, \$29, and \$49, respectively.<sup>1</sup> In addition to copayment levels, payers have also increased the copayment differentials between Tiers 1 and 2 and between Tiers 2 and 3 to more strongly

encourage the use of generics and preferred brands. The Tier 1 to 2 copay differential increased from \$7 in 2000 to \$19 in 2011, while the Tier 2 to 3 copay differential increased from \$14 to \$20.<sup>1</sup> The implementation of a fourth tier is another method for controlling prescription drug spending. Most four-tier plans have copayments for Tiers 1, 2, and 3, but coinsurance for Tier 4. This is generally due to the relatively high cost of drugs that are on Tier 4. The average coinsurance for Tier 4 was 29% in 2011.<sup>1</sup>

Several studies indicate that introducing tiered formularies and increasing copayments effectively incent plan members to switch to less expensive drugs (i.e., preferred brands or generics), thereby reducing brand-drug utilization and overall expenditure. A study by Huskamp et al. showed that when employers switched from a 1-tier formulary to a 3-tier formulary, 41.6% of enrollees taking ACE inhibitors switched to a drug of a lower tier with lower copayments. Additionally, 35.1% and 49.4% of enrollees taking proton-pump inhibitors and statins, respectively, switched to drugs with lower copayments.

However, the Huskamp study did raise an important concern. For enrollees taking a tier-3 drug at the time of a switch from a 1-tier to a 3-tier formulary, the formulary change resulted in discontinuing the use of all drugs in that class for 16.2%, 32%, and 21.3% of patients taking ACE inhibitors, proton-pump inhibitors, and statins, respectively.<sup>11</sup> Another study by Solomon et al. showed that doubling copayments for newly diagnosed hypertension, hypercholesterolemia, and diabetes patients delayed initiation of pharmacotherapy by a median of 532, 616, and 286 days, respectively.<sup>12</sup> Most estimates of price elasticity suggest that increasing a copayment by 10% reduces drug utilization by 1% to 4%.<sup>13</sup>

Drugs covered under the medical benefit provisions of commercial plans and under Medicare Part B are those administered in an outpatient setting. These drugs tend to be intravenous drugs or injectables. They are usually administered at either a physician's office or at an intravenous infusion clinic. After administering the drug, the physician's office or the infusion clinic bills the patient's payer for reimbursement for the cost of the drug and the time for infusion. Medicare patients pay a copayment for the physician's visit and a 20% coinsurance for the drug administered.<sup>10</sup> However, approximately 80% of Medicare enrollees have Medigap (i.e., private

individual health insurance to cover healthcare costs not covered by Medicare) which covers the 20% coinsurance. Thus, most Medicare patients only pay the copayment for the visit. For patients covered under commercial plans, the structure of the payments for drugs covered under the medical benefit varies widely. Some plans have no coinsurance for drugs covered under the medical benefit, while others do. However, no matter whether the patient is covered under Medicare Part B or commercial insurance, there is no system in place to incentivize doctors or patients to use lower cost therapeutics similar to the system of tiered formularies for drugs covered under Medicare Part D and the pharmacy benefit of commercial insurance.

In addition to tiered formularies, payers use other types of access restrictions to monitor and control the utilization of drugs. The three main types of restrictions are prior authorizations, step edits, and quantity limits. Prior authorizations can be applied to drugs covered under both the medical benefit and the pharmacy benefit. In general, prior authorization on a drug requires the physician who is either prescribing or administering the drug to fill out a form or call the payer in advance of treatment to obtain approval and confirmation that the drug will be covered. However, the requirements that payers put in place for the prior authorization vary widely. Some prior authorizations are simply in place to ensure that the drug is being used for an FDA approved indication. Others require the patient to have tried and failed on other less expensive drugs before receiving the drug with the prior authorization. These are simply two examples. Either way, having a prior authorization requirement on a drug deters the physician from using it because it requires the physician to do additional work. A study examining the impact of a prior authorization (PA) on pregabalin, a drug used to treat epilepsy and neuropathic pain, showed that, compared with non-PA plans, plans requiring a PA for pregabalin experienced a 5.0 percentage point lower increase in patients using pregabalin year over year. Furthermore, utilization in PA plans of other anticonvulsants was 3.7 percentage points higher than in non-PA plans.<sup>15</sup> Another study demonstrated that the implementation of a PA on non-preferred lipid-lowering statins for dual Medicare and Medicaid enrollees in Michigan was associated with an immediate 58% reduction in prescriptions of non-preferred brands and a corresponding increase in prescriptions for preferred drugs.<sup>16</sup>



Another technique payers use to encourage cost-effective prescribing is known as the step edit. The goal of a step edit is to encourage the use of therapeutically equivalent, lower-cost alternatives before “stepping up” to a more expensive therapy.<sup>6</sup> A step edit can only be placed on drugs distributed via retail pharmacies, since under a step edit a pharmacy automatically switches one drug out for another at the point of dispensing. This is not possible for a drug administered at a physician’s office because the physician first gives the patient the drug and then bills the insurance company or Medicare. Thus, the insurance company or Medicare does not have the opportunity to switch out one drug for another. With a step edit, electronic messaging is sent directly to the pharmacist from the patient’s payer’s adjudication computer system to switch the drug for a different one.<sup>6</sup>

Step edits are very effective at reducing cost. For example, a study which looked at implementing a generics first initiative for antidepressants found that placing a step edit on all branded antidepressants resulted in a 13% decrease in antidepressant drug cost, from \$4.16 PMPM (per member per month) to \$3.62 PMPM. Overall, implementing a step edit on all branded antidepressants requiring patients to first try and fail a generic before moving to a branded drug saved this insurer approximately \$1.9 million in 2005.<sup>7</sup> Another study analyzed the financial impact of a step edit for angiotensin receptor blockers (ARBs) requiring prior use of angiotensin-converting enzyme inhibitors (ACEIs). These are two classes of drugs commonly used to treat hypertension. The study found that the average cost per day of antihypertensive drug therapy was 12.8% lower in the step edit group compared to the group of patients without step edits.<sup>8</sup>

Quantity limits are the least complex technique used by payers to manage appropriate utilization of drugs. A quantity limit prevents a retail pharmacy from dispensing more than a specified amount of a drug for a given period time. For physician-administered drugs, a quantity limit prevents the physician from receiving reimbursement for more than a specified amount of the drug for a given period of time. This incentivizes the physician to not administer more than that amount to the patient. In general, the goal of quantity limits is to prevent overuse of drugs. Thus, they are most often implemented on drugs prone to over utilization such as opioids for pain. However, implementing a quantity limit costs the payer money in administration and

enforcement. Thus, the payer must determine for a given drug if the cost-savings from prevention of over utilization outweigh the administrative costs of the quantity limit.

**Figure 2: Summary of Drug Utilization Techniques**

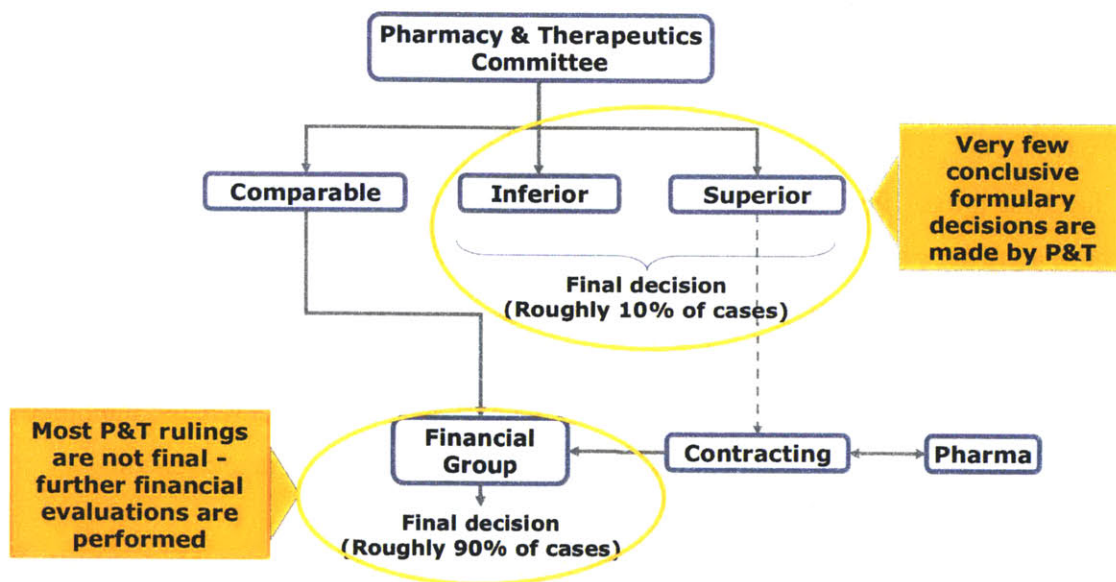
Restriction	Pharmacy or Medical Benefit	Purpose
<b>Tiered Formulary</b>	Pharmacy Benefit only	Steer members to generics and preferred brands
<b>Prior Authorization</b>	Medical and Pharmacy Benefit	Widely varies
<b>Step Edit</b>	Pharmacy Benefit only	Switches out the prescribed drug for another drug at the pharmacy
<b>Quantity Limit</b>	Pharmacy Benefit only	Limits the amount of drug distributed/administered

### ***Drug Coverage Process***

The process for making coverage decisions—deciding what drugs a payer will cover and what ones it will not—is similar across insurers. Every insurer has a pharmacy and therapeutics (P&T) committee. Usually, this committee is composed of physicians, pharmacy directors, and medical directors. The committee decides whether a drug should be covered, and in some cases, at what level a drug should be covered. Additionally, every insurer has a contracting group. The contracting group is responsible for negotiating pricing with pharmaceutical companies. For some plans, the P&T committee is shown the contracting information before making its coverage decisions. For the majority of plans, though, the P&T committee is not shown any contracting information. Rather, this information is incorporated after the P&T committee makes their decision.

The P&T committee usually rates a drug as superior, inferior, or comparable. Drugs that are declared superior are automatically added to the formulary. Those that are declared inferior are not added to the formulary. Only about 10% of all drugs are rated superior or inferior by most P&T committees. Most drugs are rated comparable and are sent to the contracting group which then determines whether and how to cover the drug based on the contracting group's ability to obtain a good price. Figure 3 summarizes the drug coverage process.

**Figure 3: General Drug Coverage Review Process**



The contracting relationship between payers and pharmaceutical companies is complex. Pharmaceutical companies contract with payers to obtain better access for their drugs. Multi-tier formularies and other drug utilization management techniques such as step edits result in payers having increased bargaining power to negotiate rebates with drug manufacturers by guaranteeing an increased volume of prescriptions for preferred drugs.<sup>11</sup> Thus, pharmaceutical companies are willing to offer payers rebates for better access and thus, increased volume. However, this type of contracting only occurs for drugs that do not already have good access. For example, drugs in areas of high unmet need such as epilepsy tend to already be placed on Tier 2 without any additional access restrictions. Thus, the pharmaceutical company has no incentive to contract because it cannot achieve any better access than it already has. However, for other therapy areas

with many drugs on the market that are considered comparable, such as statins, payers will place the most expensive drug on the highest tier and possibly have additional restrictions such as step edits. As a result, the pharmaceutical companies are incentivized to contract with payers for better access for these drugs. These contracts can take many forms. The most common is a straight rebate on the list price of the drug for better access. Other types of contracts such as bundling exist as well. Bundling is when a pharmaceutical company offers a rebate on one or several drugs, but requires that all drugs receive preferred access. In other words, access for each individual drug is not negotiated independently.

As expected, pharmaceutical contracts with payers are highly confidential because pharmaceutical companies do not want one payer demanding to receive the same rebate as another payer. Thus, it is difficult for the public to fully comprehend what payers are actually paying for these drugs. If payers were more open about the details of the contracts, the public would have a greater understanding around pricing and coverage issues. There would also be greater visibility into the specifics that determine how payers cover a drug, such as the importance of efficacy versus contracted rebates. As a result, the confidentiality of these contracts makes it very difficult for the public to truly understand the impact rebates and other pricing approaches from pharmaceutical manufacturers have on their coverage decisions.

### ***Physician Incentives***

Physicians have varying, but limited, financial incentives to control overall drug costs. The types of incentives depend on whether the physician is prescribing a drug covered under the pharmacy benefit of an insurance plan or administering drugs under the medical benefit. In general, physicians have no direct financial incentives for drugs covered under the pharmacy benefit. Yet, some creative approaches have been tried to incent physicians to control prescription drug costs.

One approach involves negotiated capitation agreements between physician groups and payers. In these circumstances, the payer sets a per member per month (PMPM) drug cost goal for the physician group. If the physician group manages to achieve a lower PMPM drug cost, then they are financially rewarded. But if their PMPM drug cost is higher than the negotiated per capita

amount, they lose money. This approach attempts to shift the decision-making process to physicians with an incentive to hold down costs. However, the technique is relatively rare because most physician groups are not large enough to effectively manage the risk associated with this approach.<sup>28</sup>

For drugs covered under the medical benefit provisions of a plan, the method of physician reimbursement can impact drug selection. Generally, physicians are reimbursed by payers based on the sales price of the drug plus a certain percent. For example, Medicare reimburses physicians for the average sales price (ASP) of the drug plus 6%. Therefore, theoretically, a physician is financially incentivized to prescribe higher priced drugs because they will earn a greater absolute value. Traditionally, Medicare reimbursement was based on average wholesale price (AWP) minus X%, not the physician's purchasing cost of the therapeutic agent. This approach allowed physicians to make a significant profit on the drug itself because physician groups negotiated with wholesale distributors for lower prices than AWP.<sup>9</sup> Thus, physicians could make a very large amount of money on the administration of drugs. Although the switch to ASP plus X% may have hurt the profitability of this reimbursement approach, physicians are still financially incentivized to prescribe more expensive drugs.

A more subtle incentive for doctors may lie in their relationship with pharmaceutical companies. Sales representatives from pharmaceutical companies spend significant time and energy with physicians promoting their companies' drug portfolio. While there are no direct financial incentive arrangements between physicians and pharmaceutical companies, there have been concerns that gifts from sales representatives impact physician behavior regarding drug utilization. To address this concern, PhRMA, the drug industry's trade and lobbying group, issued stringent guidelines in 2008 that prevent pharmaceutical companies from giving physicians excessive gifts.<sup>29</sup>

### ***Coverage of Intravenous Oncologics***

Intravenous (IV) oncologics are an example of drugs that are covered under Medicare Part B or the medical benefit of commercial plans. An important aspect of oncologics is that they are one

of Medicare's six protected classes of drugs. In 2006, Centers for Medicare and Medicaid Services (CMS) specified six "protected" classes of drugs—antidepressants, antipsychotics, anticonvulsants, antiretrovirals, immunosuppressants, and oncologics. The protected classes originated from a review of formularies of comparable drug programs, such as Medicaid and the Federal Employees Health Benefit Program, which showed that for clinical effectiveness, patients taking these drugs require uninterrupted utilization. Additionally, there was some concern that plans would not cover these drugs due to their relatively high costs.<sup>22</sup>

CMS requires health plans to cover "all or substantially all" of the approved drugs in each of the six classes.<sup>22</sup> The wording "substantially all" is purposely vague. Some interpret it as requiring plans to cover all drugs at the lowest copayment, while others believe it allows for payers to still manage the classes with step edits, prior authorizations, and quantity limits. Either way, it results in a conversation between the payer and CMS regarding the coverage of drugs in these classes. The Medicare Prescription Drug Simplification Act of 2006, section 112, extended the requirement of covering "all or substantially all" of the drugs in the six protected classes for additional years.<sup>22</sup>

Another strong impact on the coverage of oncologics is the high level of unmet need and the political sensitivity of the therapy area. Payers face a large amount of public pressure to make all drugs in the oncology space available to patients.<sup>23</sup> The patient advocacy groups for various types of cancer are incredibly vocal and strong with respect to drug coverage. Additionally, for most types of cancer there are very few or no alternative treatment options, which makes it even more difficult for payers to deny access to the limited available treatment options.<sup>23</sup>

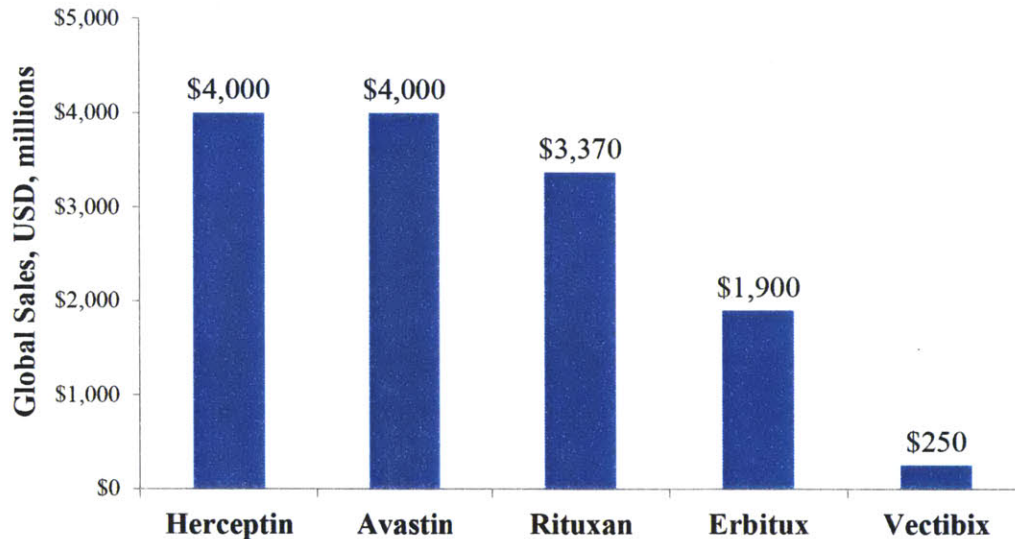
As many of these drugs have sales of over \$1 billion annually, access and coverage of intravenous oncologics is financially important to payers and manufacturers. Figure 4 presents annual sales amounts for the top intravenous oncologics.<sup>40</sup> The variance in sales between the different oncologics is due to a combination of the size of the specific cancer market the drug has been approved for, the number of indications, the price of the drug, and how early in the treatment paradigm the drug is used. The overall cancer market was estimated at \$45 billion in 2006 and currently represents over 7% of global pharmaceutical sales. Rough estimates indicate



that over 1 million new cases of cancer are diagnosed in the US per year, and approximately 500,000 people die of cancer annually, making cancer the second leading cause of death.<sup>41</sup>

#### **Figure 4: 2009 Global Sales of Intravenous Oncology Drugs**

Source: BCC Research – Biologic Therapeutic Drugs



Finally, off-label use of drugs in oncology is a significant issue. When pursuing FDA approval for an oncology drug, the pharmaceutical companies must select a specific type of oncology to target for its approved label (e.g., metastatic renal cell carcinoma or HER-2 positive metastatic breast cancer). However, sometimes an oncology drug's mechanism of action suggests that it would be effective in treating other cancer types besides the one for which it was approved. Physicians will frequently try various non-indicated oncology drugs for different types of cancers, but there can be a problem as to whether the payers will pay for this. Due to the increasing price of drugs, payers are becoming more and more hesitant to pay for off-label use of oncologics. The sum total of these coverage issues makes IV oncologics a particularly complex class of drugs.

### ***Coverage of Fixed Dose Combination Drugs***

Fixed dose combination drugs are interesting because their value is often questioned by payers, and thus, they tend to encounter significant access restrictions. A fixed dose combination (FDC) is a combination of two or more FDA-approved drugs at given doses. Therapy areas in which fixed dose combination drugs are used include the prevention of cardiovascular disease, hypertension, asthma, diabetes, and HIV/AIDS. The rationale for use of fixed dose combination drugs varies by therapy area. For example, FDC drugs for blood pressure are used because two drugs, each typically working at a separate site, block different blood pressure pathways. Additionally, the second drug of the combination may check counter-regulatory system activity triggered by the other.<sup>24</sup>

One universal argument for the use of FDCs is increased compliance, since FDCs combine two drugs into a single dosage. Only having to take one pill can increase a patient's likelihood of remaining compliant with their medication. A study by Bangalore et al. showed that fixed dose combinations reduce the risk of non-compliance by 24-26%.<sup>46</sup> This is particularly pertinent in the treatment of blood pressure where compliance has been a major issue. The fixed dose combination drugs for blood pressure have been shown to offer equivalent or better efficacy than monotherapy, and offer an improved chance of increased compliance.<sup>25</sup> Fixed dose combinations of anti-retroviral therapies have also improved efficacy. Prolonging anti-retroviral regimen durability is very important to achieving long-term treatment success for HIV patients because successive antiretroviral regimens have shown progressively shorter durability. Studies have shown that once-daily fixed dose combination anti-retroviral therapies significantly increase the length of therapy duration.<sup>47</sup>

A strong motivation for producing a fixed dose combination drug for a drug manufacturer is to extend the patent life of a drug that is about to lose patent exclusivity. A manufacturer can obtain a patent for the combination of two generic drugs. As a result, the manufacturer is still able to command market exclusivity for the fixed dose combination and thus, can price the product at the level of branded drugs, rather than generics.

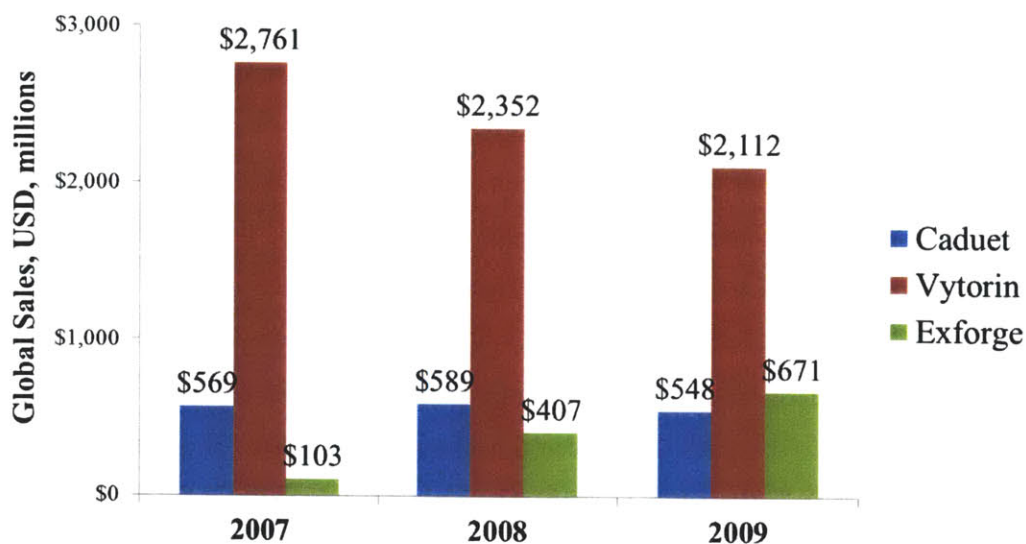


On the other hand, many physicians and payers are skeptical about the benefits of fixed dose combination drugs. Physicians are concerned about the inability to adjust the dose of one of the elements of the combination drug individually. Also, differing pharmacokinetics of the drugs might cause an issue with the frequency of administration.<sup>26</sup> Since fixed dose combination drugs are frequently a method of extending a drug's patent and thus maintaining a high price for the drug, most payers do not see the value of the fixed dose combination over taking each of the cheaper drugs separately. Rather, payers tend to consider FDCs life-style drugs that provide convenience rather than drugs that increase survival. A case in point is fixed dose combinations developed to prevent tuberculosis, but which had significant difficulties obtaining coverage in the US. These FDCs were recommended by WHO and the International Union Against Tuberculosis and Lung Disease because they simplify prescribing the drugs, and have the potential to limit the risk of drug-resistant tuberculosis arising as a result of inappropriate drug selection and monotherapy.<sup>45</sup> However, these FDCs to prevent tuberculosis have received little uptake in the US due to the lack of coverage by payers. In general, many payers regularly place stringent access restrictions on fixed dose combination drugs. Though the efficacy of FDCs is rarely questioned, the added value of FDCs is often not considered to be better than the alternative of taking each drug individually.

Despite the criticisms of FDCs, cardiovascular fixed dose combination drugs have the potential to be billion dollar molecules. Vytarin had over \$2 billion in sales for 2007, 2008, and 2009. Exforge, which just launched in 2007, is projected to have over a \$1 billion in US sales annually by its peak. Figure 5 provides detailed sales numbers. Although these are significant sales levels for individual drugs, they represent a small portion of the total cardiovascular market, which is estimated at \$144 billion in 2010. Cardiovascular drugs are the largest selling class of drugs, mainly because heart disease/stroke is the leading cause of mortality globally.<sup>39</sup>

## Figure 5: Annual Sales of Fixed Dose Combination Cardiovascular Drugs

Source: BCC Research – Cardiovascular Therapeutic Drugs

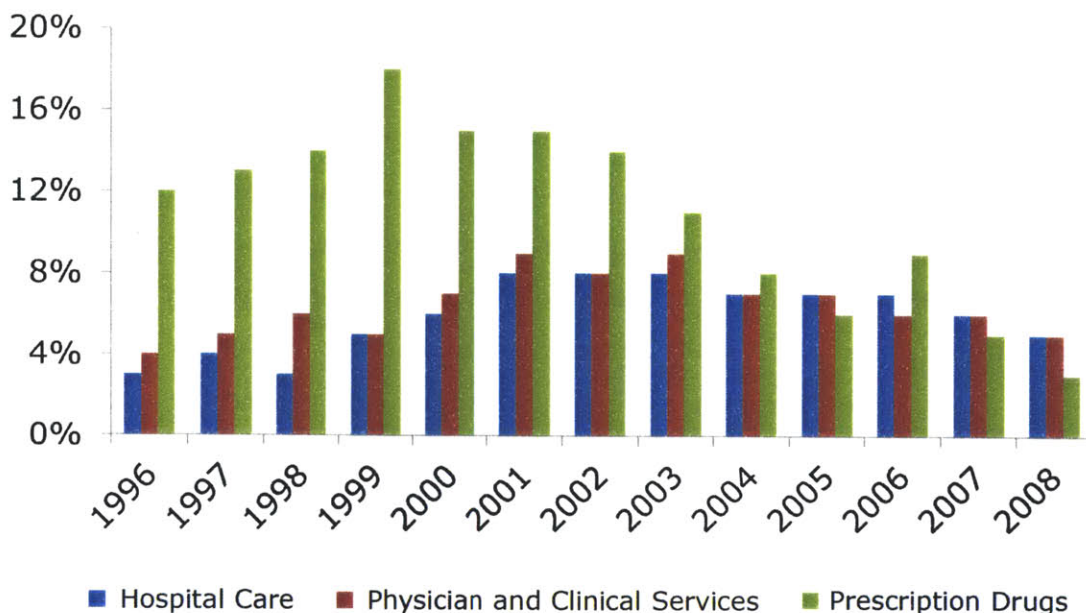


### *Growing Concern over Drug Prices*

In light of rising pharmaceutical costs, the aging population, and the increased use of costly specialty drugs, the escalation of drug costs is a growing concern in the U.S. Although drugs represent only a small portion of the U.S.'s overall healthcare spending (~10%), they have been the fastest growing segment of the healthcare market in the U.S. over the past 15 years (see Figure 6). Both increased utilization and price increases have contributed to the increase in overall drug spending. The number of prescriptions bought in the U.S. increased by 39% from 1999 to 2009. Retail prescription prices increased on average 3.6% annually from 2000 to 2009, while the average inflation rate was only 2.5%. This cost escalation has resulted in many people calling for the government to take a more active role in negotiating drug prices. However, opponents believe that government intervention could have unintended consequences such as stifling drug innovation and negatively impacting patient care.<sup>17</sup>

## Figure 6: Annual Percentage Increase in US Health Expenditures

Source: Kaiser Family Foundation calculations using National Health Expenditures data from Centers for Medicare and Medicaid Services



To address the concern about the growing drug expenditure, payers continue to implement new techniques for reimbursement. As mentioned previously, many prescription drug plans have introduced a tier 4 for relatively high-cost specialty drugs or lifestyle products. Tier 4 drugs have a coinsurance requirement (averaging 29%) instead of the flat copayment found in Tiers 1, 2, and 3. Medicare has been particularly aggressive in introducing a Tier 4. Among Medicare Part D payers in 2008, 87% of plans have a Tier 4 for specialty drugs, while only 7% of workers covered by commercial plans have a Tier 4.<sup>21</sup> Some plans are now experimenting with having a Tier 5 so that they can distinguish between preferred specialty drugs (Tier 4) and non-preferred specialty drugs (Tier 5). Tier 5 drugs would have a higher copayment or coinsurance than Tier 4 drugs.<sup>21</sup>

Another burgeoning technique to control drug spending is switching physician-administered drugs from the medical benefit to the pharmacy benefit. This would allow payers to have significantly more control over the use of the drugs. However, for this to occur, physicians would have to receive their drugs via a specialty pharmacy that the payer is contracted with or owns.

Thus, the physician would no longer be purchasing the drugs independently and billing the payer for reimbursement. WellPoint has already begun to require members to obtain certain drugs through their specialty pharmacy which is part of their in-house pharmacy benefits manager (PBM) NextRx.<sup>21</sup>

In recent years, drug prices for oncologics have received significant attention due to the large number of cancer drugs in development and the launch within the past 10 years of some relatively highly priced oncologics such as Avastin, Vectibix, and Provenge. Avastin initially launched in 2004 for the treatment of metastatic colorectal cancer with a monthly cost of \$4,400. Genentech, the manufacturer of Avastin, came under fierce criticism from physicians and patients in 2006 for Avastin's cost when it received approval for the treatment of metastatic non-small-cell lung cancer (NSCLC). The monthly treatment cost for Avastin to treat NSCLC at that time ranged up to \$8,800 per month or over \$100,000 per year.<sup>18</sup> Avastin is an IV oncologic, meaning that it is covered either under Medicare Part B or the medical benefit of commercial plans for patients. Some patients have a 20% coinsurance associated with drugs covered under the medical benefit, with no out-of-pocket limit. Thus, these patients could have paid over \$20,000 per year just for Avastin. As a result of the public outcry, Genentech decided to cap the total cost of Avastin at \$55,000 for patients below a certain income level. However, there was still concern over Avastin's price because in clinical trials for NSCLC, it appeared to increase survival by only two months, from a median of 10.3 months to 12.3 months.<sup>18</sup>

The launch of Provenge by drug manufacturer Dendreon is another example of the challenges facing relatively highly priced oncologics. Provenge's \$93,000 price tag caused CMS to launch a national coverage review just two months after its launch in 2010. National coverage reviews are very rare and hardly occur so soon after launch. The director of the Coverage and Analysis Group at CMS, Louis Jacques, stated that "While the cost of Provenge was not an issue in our coverage determination, I think it is fair to say that the cost of Provenge created a public buzz around this particular product, which then made it a higher-profile issue and something that we should look at."<sup>20</sup> The result of CMS's national coverage review was that each payer would be allowed to determine on its own whether and how to cover Provenge, even though Provenge is an oncology treatment and thus, included in one of Medicare's six protected classes.

Though the costs of Avastin and Provenge may seem high, the development costs and timelines to bring a new drug to market in general are significant and increasing. Estimates for the cost of bringing a new drug to market range from \$800 million to over \$2 billion. Although the exact amount of money that is required to develop a drug is debated, all experts agree that development costs are rising rapidly.<sup>44</sup> As a result, pharmaceutical manufacturers need to generate more revenue to be sustainable. In particular for oncology drugs, the availability of effective treatments has made it difficult for manufacturers to recruit patients for clinical trials. At the same time, payers have been demanding overall survival data. These two aspects have extended the amount of time to get an oncology drug to market.<sup>42</sup> Adams et al. estimated that it costs over \$1 billion dollars to bring an oncology drug to market due to the low success rates and long duration of clinical trials. In this study, oncology was the second most expensive therapy area in which to develop a drug.<sup>43</sup> And, this does not take into account the opportunity costs that companies are incurring by investing their money in risky drug development. Finally, the manufacturing and regulatory costs for biologics, which include most branded intravenous oncologies, are very high compared to small molecule drugs. Companies manufacturing biologics need to obtain manufacturing approval from the FDA for every single plant. Additionally, the synthesis process of a biologic is significantly more cumbersome and thus, more expensive when compared to the manufacturing of a small molecule. Given these risks and costs, one may consider the recent increases in prices of drugs justified.

The controversy over drug prices raises the issue of why pricing of drugs is different from pricing in other industries. For most other industries, the U.S. relies on competitive markets to align prices with value to consumers and cost to producers. However, there are several aspects of the pharmaceutical market that interfere with this ideal. First, the patenting of drugs creates an exclusive environment where there is no competition and thus, no alternative for consumers to select. Second, insurance companies are in the middle of healthcare interactions, shielding the consumer from the actual cost of healthcare. This makes the consumer less price sensitive because he/she is not seeing the full extent of pricing.<sup>19</sup> Finally, many healthcare situations are life and death. It is very hard for our American society to admit that the life of an individual is only worth a finite amount of money. However, in some other countries such as Canada and the

UK, society is stating that their healthcare system is only willing to pay a certain amount for value. In the UK, this is in the form of cost per quality-adjusted life year (QALY). If a drug exceeds a set cost per QALY, the government's universal healthcare system does not cover it.

In the U.S., a key question is what further can be done to control drug costs? And how will these cost containment techniques vary by drug class? IV oncologics are included in one of Medicare's six protected classes, are reimbursed via Medicare Part B or the medical benefit of commercial plans, and are politically a very sensitive topic. Given these factors, how will the growing costs of oncology drugs be addressed? In contrast, fixed dose combination drugs for cardiovascular disease have questionable value, are managed by Medicare Part D plans or the pharmacy benefit of commercial plans, and have less immediate survival consequences. As a result, will the U.S. healthcare system determine that it will not pay a premium for them?

## **Chapter 3: Thesis Objective and Methodology**

### ***Thesis Objective***

Increasing drug prices have been and continue to be a major issue in the U.S. Typically, payers are responsible for reigning in healthcare costs in the U.S.'s employer-based healthcare system through the implementation of utilization management tools. These utilization management tools drive members to lower cost drugs, and thus, deter pharmaceutical companies from pricing drugs too high. The objective of this thesis is to identify the relative importance of the factors considered by payers to be important in drug reimbursement and, specifically, to examine the role price plays. To do this, we chose two very different classes of drugs: cardiovascular fixed dose combination drugs and intravenous oncologics. This selection allows us to assess the role of pricing for a set of drugs that are of questionable benefit and reimbursed under the pharmacy benefit (FDCs), and a set of drugs that are highly political and reimbursed under the medical benefit (IV oncologics). We can then infer whether pricing plays an important role for coverage of all drugs or if its role varies depending on the class of drugs. Secondly, we explore the utilization techniques used by payers and examine if altering the price of any of these drugs would improve access and thus, overall sales.

### ***Literature Review***

An extensive review of the literature was conducted to understand the pricing and coverage of the select drugs as well as to gain an understanding of the factors that contributed to payers' decisions regarding these drugs. The Red Book provided the list prices for all of the select drugs. Medicare's Formulary Finder program allowed us to obtain the formulary coverage of the select drugs for fifteen different Medicare plans including nine large national plans and five regional plans. FDA regulatory submissions included on the FDA's website were used to obtain specific indications for each of the select drugs as well as information regarding their clinical trials. Drug websites and their prescribing inserts were analyzed to determine the dosing regimen and associated overall cost for the IV oncologics. Additionally, numerous articles and papers in the mainstream media, scientific journals, and other media outlets were used to gain a strong

background regarding how payers are currently attempting to manage drug prices and utilization as well as the impact of high drug costs on the public.

### ***Interview Guides***

To assess the hypothesis that drug pricing is a driving factor in the coverage decisions of cardiovascular fixed dose combination drugs and intravenous oncologics, two interview guides and a pre-interview questionnaire were created. The pre-interview questionnaire was designed to obtain facts from payers specific to their company prior to the interview in order to better use the interview time. Additionally, the pre-interview questionnaire allowed us to address during the interview more specific questions around coverage decisions. The interview guide for payers examines not only the role of pricing in coverage decisions, but also the role of other factors in the process so we could obtain an understanding of the relative importance of pricing. These interview guides are a combination of quantitative and qualitative questions to allow for comparison across discussions and to obtain more substantive results. The interview guide for the oncology drug distributor is composed of qualitative, open-ended questions in order to better understand the role drug distributors play in attempting to control drug prices.

### **Payer Pre-Interview Questionnaire:**

1) Number of lives your plan covers:

	<b>Commercial Lives</b>	<b>Medicare Lives</b>
<b>Medical Benefit / Part B</b>		
<b>Pharmacy Benefit / Part D</b>		
<b>Total</b>		



2) Average copay amount (\$) :

	<b>Commercial Plan</b>	<b>Medicare Plan</b>
<b>Tier 1</b>		
<b>Tier 2</b>		
<b>Tier 3</b>		
<b>Tier 4</b>		
<b>Tier 5</b>		

3) Your plan's coverage of the following drugs. Examples of restrictions are step edits (SE), prior authorizations (PA), and quantity limits (QL):

	<b>Commercial</b>		<b>Medicare</b>	
	<i>Tier</i>	<i>Restrictions</i>	<i>Tier</i>	<i>Restrictions</i>
<b>Caduet</b>				
<b>Vytorin</b>				
<b>Exforge</b>				
<b>Provenge</b>				
<b>Erbitux</b>				
<b>Vectibix</b>				
<b>Avastin</b>				

#### **Payer Interview Guide:**

- 1) Please elaborate on the details of each of the prior authorizations and step edits for each of the drugs.
- 2) On a 5 point scale where 1 is low impact and 5 is high impact, what influence do the following factors have on formulary decisions for each of the following drugs:

- a. Does the level of impact of each of the factors differ for Caduet, Vytorin or Exforge?

	<b>Caduet</b>	<b>Vytorin</b>	<b>Exforge</b>
<i>Outcomes Data</i>			
<i>Side effects Data</i>			
<i>Physician Demand</i>			
<i>Patient Demand</i>			
<i>List Price</i>			
<i>Contracting</i>			
<i>Compliance</i>			

- 3) Please explain any differences in the coverage decisions around Caduet, Vytorin and Exforge.
- 4) Is the decision not to cover (*drug not covered*) price related?
- a. To what level would (*drug not covered*) have to lower its price to obtain coverage?
- 5) What would the pharmaceutical company have to do to obtain better coverage for (*drug not covered*)?
- 6) On a 5 point scale where 1 is low impact and 5 is high impact, what influence do the following factors have on formulary decisions for each of the following drugs:
- a. Does the level of impact of each of these factors vary for Provenge, Erbitux, Vectibix, or Avastin?

	<b>Provenge</b>	<b>Erbitux</b>	<b>Vectibix</b>	<b>Avastin</b>
<i>Time to progression</i>				
<i>Overall survival</i>				
<i>Control of symptoms</i>				
<i>Side effect data</i>				
<i>Physician Demand</i>				
<i>Patient Demand</i>				
<i>List Price</i>				
<i>Contracting</i>				
<i>Level of Unmet Need in Therapy Area</i>				
<i>Public Policies (e.g. Medicare)</i>				

- 7) Please explain any differences in the coverage decisions around Provenge, Erbitux, Vectibix, and Avastin.
- 8) Is the decision not to cover (*drug with high level of restrictions*) price related?
  - a. To what level would (*drug with high level of restrictions*) have to lower its price to obtain less restrictive access?
- 9) What would the pharmaceutical company have to do to obtain better coverage for (*drug with high level of restrictions*)?
- 10) At what level are coverage decisions made?
- 11) Is there anything historically that has happened to the company which strongly impacts how coverage decisions for any of these drugs are made?

## **Oncology Drug Distributor Interview Guide:**

- 1) Please give an overview of your business model.
- 2) Does your organization have preferred oncologics?
  - a. If yes, what is the basis for a preferred oncologic (e.g. efficacy, contracting, price, etc.)?
- 3) Please explain the genesis for your utilization management system in oncology.
  - a. What were physicians' initial reactions?
- 4) What increase in overall survival is considered significant enough to be considered a more efficacious drug?
  - a. Does the level vary by cancer type?
  - b. How about progression-free survival/time to progression?
- 5) Are convenience factors such as time of the infusion taken into account in the development of your utilization management system?
- 6) What does opting into the utilization framework entail for a physician office?
- 7) What percentage of physicians in your network has opted into the utilization framework?
- 8) What challenges have you encountered while implementing your utilization management system?

## ***Selection of Interview Participants***

There were two primary considerations in selecting participants for the payer interviews. First, we wanted a mixture of national and regional payers in order to eliminate any regional bias. Second, we targeted national and regional payers with a large number of members to obtain a

decent representation of U.S. citizens with a small sample size. Specific individuals were selected based on a combination of contacts from my professional network, suggestions from thesis advisors, and leads drawn from preceding interviews. The result was seven interviews, including three national payers, two regional payers, and two people from a large oncology drug distributor. The interview participants tend to hold positions in the pharmacy department such as pharmacy directors or vice presidents of pharmacy.

It should be noted that the goal of these interviews was not to reach a statistically significant conclusion, but rather to obtain directional information. The interviewed payers collectively cover over forty million pharmacy benefit / Part D lives and just under a hundred million medical benefit / Part B lives in the U.S., which we think is an adequate representation to answer the question posed by this thesis. We acknowledge that a larger study may be necessary to achieve a statistically significant conclusion.

The identities of those interviewed and their companies will remain confidential as the information they provided concerning how their companies operate and make decisions is highly proprietary. Also, the identity of those associated with individual responses will remain confidential.

## Chapter 4: Results

### *Summary of Literature Review and Public Sources*

In order to gain a preliminary indication of whether pricing strongly influences the coverage of fixed dose combination cardiovascular drugs and intravenous oncologics, the prices of each of the select drugs were obtained from the 2011 Red Book. For the FDCs, the prices were obtained for 30 pills since that is the number of pills a patient must take per month. As shown in Figure 7, Caduet has the highest list price followed by Vytorin and then Exforge.

**Figure 7: Fixed Dose Combination Cardiovascular Drug Pricing**

Source: Red Book 2011

Drug	Dose	Quantity	Average Wholesale Price
<b>Caduet</b>	5 mg amlodipine 10 mg atorvastatin	30 pills	<b>\$134.84</b>
<b>Vytorin</b>	10 mg ezetimibe 20 mg simvastatin	30 pills	<b>\$124.16</b>
<b>Exforge</b>	5 mg amlodipine 160 mg valsartan	30 pills	<b>\$97.06</b>

The Red Book was also used to obtain prices per vial for the select intravenous oncologics. Dosing information for each oncologic was obtained from the drug's prescription information insert. Prices were calculated by first determining the dose for an average male. Then the most cost-efficient number of drug bags was chosen to fulfill this dose. Next the list price per bag was retrieved from the 2011 Red Book. Finally, the cost was divided by the number of weeks between doses in order to obtain a weekly cost (see Figure 8).

## Figure 8: Oncology Drug Pricing Calculations for Maintenance Dosing

Source: Individual Drug Prescribing Information and Red Book 2011

Drug	Oncology Indication	Dosing	Dose per Week*	Drug Bags Required	Price per Bag	Cost per Week
<b>Provenge</b>	Prostate	3 doses at 2 week intervals	N/A	N/A	\$93,000 per dose	<b>\$46,500</b>
<b>Erbix</b>	Colorectal Head and Neck	250 mg/m <sup>2</sup> per week	475 mg	2 x 100 ml bags 2 x 50 ml bags	\$1,152 per 100 ml bag \$576 per 50 ml bag	<b>\$3,456</b>
<b>Vectibix</b>	Colorectal	6 mg/kg per 2 weeks	260 mg	3 x 5 ml bags	\$1,019 per 5 ml bag	<b>\$3,056</b>
<b>Avastin</b>	Colorectal Renal cell Non-small cell lung	10 mg/kg per 2 weeks 15 mg/kg per 3 weeks	433 mg	1 x 16 ml bag 1 x 4 ml bag	\$2,680 per 16 ml bag \$670 per 4 ml bag	<b>\$3,350</b>

\* Dose per week assumes a weight of 86.6 kg and a body surface area of 1.9 m<sup>2</sup>

It should be noted that this approach to determining the cost per week has certain limitations. For example, some infusion clinics reuse bags for different patients rather than discarding any remaining drug, though this is a rare practice. Additionally, the approach does not take into account the duration of treatment. Some of the oncologics are given to patients for over a year, such as Avastin, while Provenge is only given in three doses over a six week period.

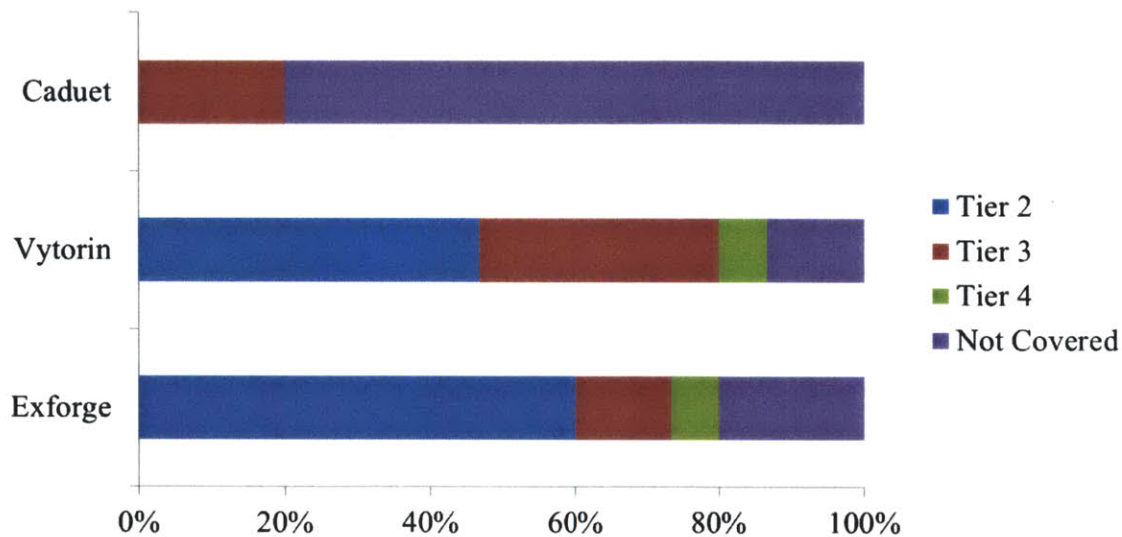
To obtain preliminary reimbursement data, we used the Medicare Formulary Finder website, which allows participants to determine the coverage of Medicare Part D prescriptions for plans in their area. Since the Medicare Formulary Finder tool presents the coverage of only Part D drugs, we were only able to determine the coverage of the select fixed dose combination cardiovascular drugs. We obtained the coverage of the FDCs for seven national payers and eight regional payers (see Appendix A for the names of the payers). As shown in Figure 9, approximately 80% of the payers did not cover Caduet, while less than 20% of payers did not cover Vytorin and Exforge. Also, those plans that did cover Caduet placed it on Tier 3. Since Caduet is the most expensive of the three FDCs, this suggests that price may be playing a role in its lack of coverage.



Additionally, Exforge, the least expensive of the three FDCs, is on Tier 2 for 60% of the payers, while Vytorin is on Tier 2 for less than 45% of payers. This suggests that Exforge's low list price may have helped it gain favorable coverage.

### Figure 9: 2011 Medicare Coverage of Fixed Dose Combination Cardiovascular Drugs

Source: Medicare Formulary Finder



Although we were unable to use Medicare Formulary Finder or any other publicly available tool to determine coverage for the select intravenous oncologics, recent articles discuss coverage and describe attempts to control the cost of these drugs. As we discussed in more detail in Chapter 2, when Avastin gained approval for the treatment of non-small cell lung cancer, there was significant public concern over the cost of the drug since the dose was increased from 10mg/kg to 15mg/kg. To assuage concerns, Genentech, the manufacturer of Avastin, placed a price cap on the drug of \$55,000 for patients below a certain income level.<sup>18</sup> Provenge, the highest priced drug of our select oncologics, has experienced the most problems obtaining reimbursement. Shortly after launch, CMS began a national coverage review.<sup>20</sup> This is very rare for an oncologic, which is one of Medicare's protected classes and, as such, plans are supposed to cover all of the drugs in that class. However, CMS's national coverage review came to the conclusion that they would allow plans to make their own decisions on how to cover Provenge.



### ***Summary of Payer Interviews***

In order to determine what role pricing plays in the coverage of these drugs, we spoke with five payers. First we asked them to review a list of factors involved in their coverage decision-making process for fixed dose combination cardiovascular drugs and intravenous oncologics and assign a score of one to five to each factor, where one is low importance in the coverage decision-making process and five is high importance in the process. Then we averaged the scores across all five payers. We also determined two weighted averages: one based on the total number of lives the payer represents, and the other based on the total number of Medicare lives the payer represents. The fixed dose combination drugs were weighted using pharmacy and Part D lives since these drugs are covered under the pharmacy / Part D benefit, while the intravenous oncologics were weighted using medical benefit and Part B lives. Payers did not vary their assigned scores by specific drug within a class (i.e., the scores for FDC's were the same, whether the payer was considering Caduet, Vytarin, or Exforge). Thus, we present our results as scores for FDCs and oncologics as two separate groups, rather than for each individual drug within each group.

Figure 10 presents the results of the scores assigned by payers. Independent of weighting, overall survival / outcomes data / time to progression played a more important role in the coverage decision-making process for oncologics than for the FDCs. Side effects data / control of symptoms, physician demand, and patient demand also all had more of an impact on coverage decisions for oncologics than for FDCs, but to a lesser degree. However, list price and contracting were much more important in the coverage decision-making process for FDCs in comparison to oncologics. In general, these comparisons hold true for all types of weighting of the data.

**Figure 10: Average Ranking of Level of Importance of Various Factors in the Coverage Decision-Making Process for FDC Cardiovascular Drugs and IV Oncologics**

	No Weighting		Weighted by Total Lives		Weighted by Medicare Lives	
	FDC	Onc	FDC	Onc	FDC	Onc
<i>Outcomes Data / Overall Survival / Time to Progression</i>	4.0	4.8	3.6	5.0	3.1	4.9
<i>Side Effects Data / Control of Symptoms</i>	4.4	4.6	4.2	4.5	4.2	4.6
<i>Physician Demand</i>	2.2	2.8	2.2	2.9	2.0	2.7
<i>Patient Demand</i>	2.4	2.8	2.2	2.9	2.2	2.7
<i>List Price</i>	4.4	2.8	4.8	2.9	4.5	3.0
<i>Contracting</i>	4.4	1.8	4.8	1.3	4.8	1.8
<i>Compliance</i>	3	-	2.5	-	3.4	-
<i>Unmet Need</i>	-	5.0	-	5.0	-	5.0
<i>Public Policies</i>	-	3.4	-	3.3	-	3.9

Payers were unanimous in the strong role pricing plays for the coverage of fixed dose combination drugs. All payers indicated that any variance in coverage of the select FDCs was based on price. That is, in order for pharmaceutical companies to obtain better coverage they would be required to lower their prices. However, payers stated that price did not impact coverage decisions for intravenous oncologics. One reason payers stated for this was that public policies such as state mandates to cover all oncologics and Medicare's six protected classes required them to cover all oncologics independent of price. Payers noted that they were limited in their attempts to manage oncologic drug utilization to prior authorizations which check that the drug is being used appropriately.

Specifically, payers mentioned that they had no mechanisms to direct appropriate patients to more cost-effective treatment pathways in oncology. One payer said that they were beginning to distribute recommended cost-effective pathways to their physicians. However, all other payers

said that there were no tools they could use to direct patients. These drugs, since they are covered under the medical benefit / Part B, are not tiered. Thus, payers cannot use patient out-of-pocket costs to incent patients to utilize less expensive treatments. Additionally, payers cannot exclude any of these drugs from their benefit plans due to public policies. Finally, payers mentioned that it is difficult even to enforce a prior authorization for these drugs, since they are distributed via group purchasing organizations to the physicians, who then bill the insurance company for reimbursement after the patient has received the drug. Payers recognize that this is very frustrating for physicians, because if a doctor gives the drug to a patient and then discovers that the indication was not covered by that patient's plan, the physician either has to pay for the drug out of his own pocket or attempt to have the patient pay for the drug.

### ***Discussion of Specific Interview Questions***

**What influence do the following factors have on formulary decisions for each of the following fixed dose combination cardiovascular drugs? Does your response vary by drug?**

All payers said their responses would not vary by drug specifically. Three out of five payers ranked outcomes data and side effects data at a level five, while the other two gave them lower rankings. However, all payers agreed that the efficacy and safety data for the fixed dose combination drugs was not particularly compelling. All respondents gave physician and patient demand a score of three or less, indicating that these factors play a small role in their decision-making process. Interestingly, payers ranked list price and contracting at a similar level of importance as outcomes and side effect data. However, payers were split on the level of importance of compliance with these drugs. Three payers considered the compliance benefits of fixed dose combination drugs to be a strong factor in their reimbursement decision-making process, while two payers did not value the compliance aspect of fixed dose combination drugs. One of the payers indicated that they value going from a twice per day pill to once per day, but that if a person can take two pills once per day then there is limited benefit to taking one pill once per day. Please see Figure 11 for details.

## Figure 11: Relative Importance of Factors in Coverage Decisions for Cardiovascular FDCs

(Example: "Outcomes Data" received one score of 2, one score of 3, and three scores of 5)



**Please explain any differences in the coverage decisions around Caduet, Vytorin and Exforge.**

Four out of five payers had differing coverage for Caduet, Vytorin, and Exforge. Three out of the four payers with varying coverage said the dominant reason for the differences in coverage is related to price and contract. Respondents stated that the drug for which they could obtain the lowest price through a discount based on their list price was placed on a favorable tier. However, most of the payers stated that other factors have some influence on coverage, including utilization data, physician demand, number of members taking the drug, and number of generics in the class. One payer said they would strongly reconsider placing a drug on a higher tier if a large percentage of their members were on the drug, because they do not want to disrupt the care of their members.

**Are the coverage decisions price related? To what level would a non-preferred drug have to lower its price to obtain better coverage?**

All payers stated that price had a strong impact on their coverage decisions for these fixed dose combination cardiovascular drugs. One payer does not cover any of the fixed dose combination drugs because they value affordability and do not see any benefit in taking one pill once per day rather than two pills once per day. Two payers stated that to obtain better coverage, the drug would have to price at the level of its individual components or slightly lower because by having members purchase one pill versus two they are losing a copay. Two other payers stated a non-preferred drug would have to lower its price to the level of the competitor FDCs. One payer stated it did not matter how low they priced the drug because there are too many generics available in this therapy area.

**What would the pharmaceutical company have to do to obtain better coverage?**

Two payers stated that the only way to obtain better coverage would be to lower the price. Another payer stated that the FDC would have to show improved efficacy and/or safety data compared to its competitors, while a different payer stated if they were able to clinically demonstrate increased compliance then they would consider offering the drug better coverage. Finally, one payer stated there was nothing to be done because there are too many generics available.

**What influence do the following factors have on formulary decisions for each of the following intravenous oncologics? Does your response vary by drug?**

All payers said that the level of unmet need in a therapy area was a very important factor in the decision-making process for intravenous oncologics. Additionally, time to progression, overall survival, control of symptoms, and side effects were given a score of four or five by all payers. Most payers thought physician and patient demand played a role in their coverage decision-making process, but not a strong one. Four out of five payers said that contracting was not a factor for this therapy area, because the pharmaceutical companies would not offer a price lower than their list price for this class of drugs. However, one payer gave contracting a score of five, indicating that this payer did have contracts with pharmaceutical companies for at least one of these drugs.

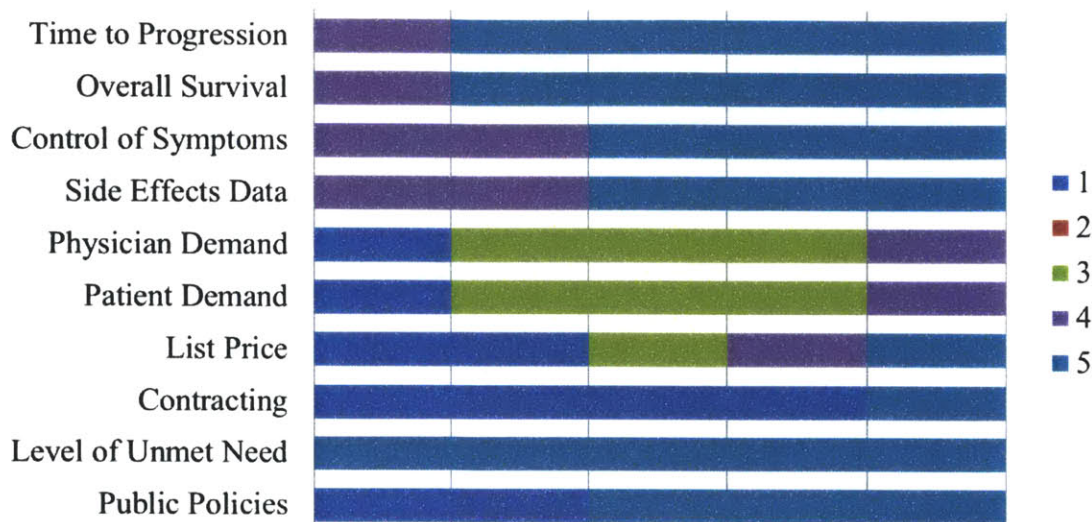


Payers were split on the level of importance of public policies. Public policies include factors such as oncology being one of Medicare's six protected classes and state mandates that require payers to cover oncology drugs for all possible indications. Some states require payers to cover all uses of oncologics including off-label use, while others only require coverage of oncologics for FDA approved indications. As a result, regional payers in states with oncology coverage mandates ranked the importance of public policies as very important, as did payers whose member population is predominantly Medicare patients. However, payers in states without oncology mandates and with a predominantly commercial membership make-up did not feel that public policies played any part in their coverage decision-making process for oncologics.

There was a wide range of responses regarding the importance of list price in the coverage decision-making process. Two payers stated that list price did not factor into their decision-making process because they are already mandated to cover all of these drugs due to certain public policies. Two other payers stated that list price was important in the decision-making process, but not as important as other factors such as overall survival and time to progression data. One payer stated that list price was very important in their coverage decision-making process, because given efficacy and safety equivalency, they work with their physicians to promote the use of the most cost-effective drugs in oncology. Figure 12 presents the detailed ratings for IV oncologics.

## Figure 12: Relative Importance of Factors in Coverage Decisions for Intravenous Oncologics

(Example: "Time to Progression" received one score of 4 and four scores of 5)



**Please explain any differences in the coverage decisions around Provenge, Avastin, Erbitux, and Vectibix.**

All of these drugs are covered under the medical benefit, so there is no variance in co-payment or co-insurance for these drugs. The only variance in coverage of these drugs were which ones require prior authorizations checking that the drug is being used for an FDA approved indication or for an indication for which there is data indicating its efficacy. Only two payers have a variance in the coverage of these drugs. The rationale was that the payers were in the process of implementing prior authorizations for all of these drugs, but they started with the ones for which they were most concerned about off-label use.

**Are the coverage decisions price related? To what level would a non-preferred drug have to lower its price to obtain better coverage?**

Three payers said that price played little to no role in the coverage decision-making process due to public policies mandating they cover all drugs in this class. One payer said that price plays an

indirect role in their coverage decision-making process. For a drug with a high prevalence, the payer may require a prior authorization to make sure there is no leakage or inappropriate use. List price has an indirect effect because it affects the overall cost.

In contrast, one payer stated that list price plays an important role in their coverage decision-making process. If a new cancer agent launches into a therapy area with no other treatment options, then this payer will cover the drug regardless of the list price or contract. However, all things being equal, the payer is working with their oncologists to create and follow cost-effectiveness guidelines. Over the past five years they have started making active comparisons for therapy areas with more than one oncologic option. The recent implementation of electronic health records has allowed them to do these analyses. They can compare overall survival for various treatment pathways, and if there is no difference they can recommend the least costly treatment pathway.

**What would the pharmaceutical company have to do to obtain better coverage?**

Besides the one payer which is issuing guidelines recommending the most cost-effective treatment pathway, all the payers stated there was nothing pharmaceutical companies could do to obtain better coverage because all of the oncologics are already covered for all FDA indications.

***Summary of Interviews with Oncologic Distributor***

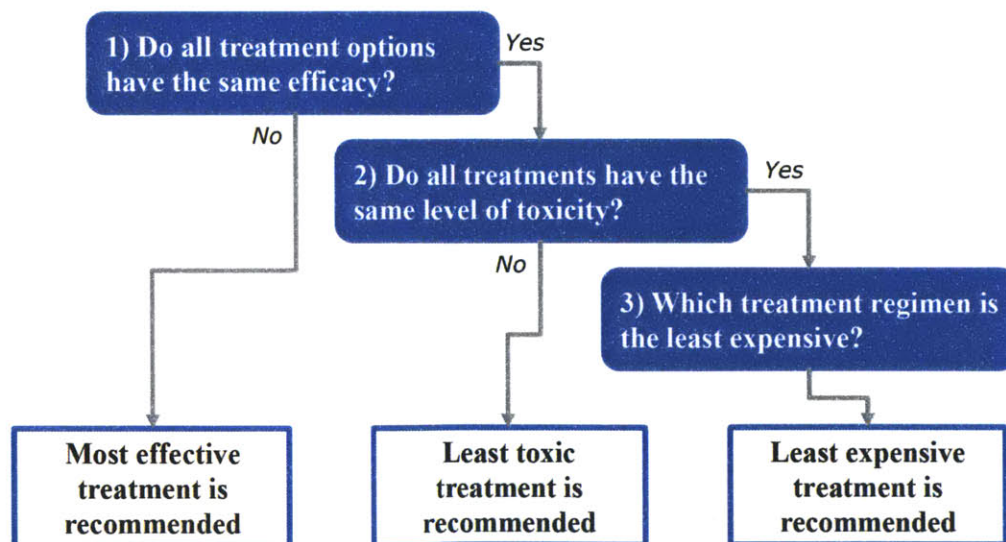
The oncologic distributor interviewed has a network of about 3,000 oncologists for which they distribute drugs. For approximately 1,000 of these physicians, the distributor also manages the physician office's IT, billing, and other back office operations. The bulk of the distributor's revenue (70-80%) derives from drug distribution and managing physicians' offices, while the rest of its revenue comes from research and other partnerships with pharmaceutical companies. Their network of physicians is growing by 5-10% per year. When searching for growth opportunities, the distributor looks for practices that are independent, have evidence-based practices, and are growth oriented. The distributor's network is predominantly in the South, Midwest, and West, and located in smaller cities that are not dominated by teaching hospitals.



In response to physicians' concerns that they could not sustain their business given the escalating costs for therapeutics, the distributor created a set of guidelines about six years ago with the goal of decreasing costs while maintaining strong outcomes data. The guidelines are evidence-based, cost-effective treatment paradigms specific for different types of cancer.

When creating a new treatment guideline, the distributor uses the decision tree in Figure 13 to decide whether to include a drug in the guidelines. Efficacy and toxicity equivalency decisions are made by the distributor's pharmacy and therapeutics committee, which is composed entirely of in-network physicians. When making efficacy decisions, overall survival data is considered the gold standard. Convenience is not taken into account specifically at any point in the process. Once a treatment guideline is created, it is sent to all of the physicians in the network prior to implementation. Individual physicians have the opportunity to vote and/or suggest changes.

**Figure 13: Oncologics Distributor's Process for the Creation of Oncology Treatment Guidelines**



At this point, the distributor has created 19-23 treatment guidelines for different types of cancer, which account for ~90% of all cancer patients. Each physician practice has the choice of opting into using the treatment guidelines. However, the physician practice must be fully managed by

the distributor for guidelines to be implemented, because the guidelines require the distributor's IT system. Eighty-five to ninety percent of the distributor's 1,000 fully-managed physician practices have opted into using the cost-effective guidelines. For these practices, the distributor has a compliance rate with the guidelines of ~80%.

The guidelines are built into the physician office's IT system, which is managed by the distributor. When an oncologist enters information about a patient into the system, three items appear:

- 1) Research papers discussing the various treatment regimens,
- 2) Clinical trial research on each of the possible treatment regimens, and
- 3) The distributor's guidelines' choice of treatment regimen.

Compliance with the guidelines is independently regulated by each individual physician practice. Some practices have implemented a process that requires physicians to send an email to the head of their physician practice if they choose a different regimen than the guidelines recommend.

Pharmaceutical companies have absolutely no influence on the treatment guidelines. The distributor does not contract with pharmaceutical companies to gain better access.

Pharmaceutical companies do not provide any research papers when the distributor is deciding on the guidelines. Pharmaceutical companies do not know whether their product is included in the guidelines. The cost-effective treatment guidelines are kept highly confidential.

## Chapter 5: Discussion

With this study, we examined the role pricing plays in the insurance coverage of pharmaceuticals in the U.S. Initially, we performed significant background research on the reimbursement structure for various formulations of pharmaceuticals. Based on this research, we decided to choose three fixed dosed combination cardiovascular drugs and four intravenous oncology drugs to examine further. These two classes were chosen because they differ in a fundamental way. The FDC cardiovascular drugs are covered by the pharmacy benefit provisions of healthcare plans and are in a less politically sensitive therapeutic area, while the intravenous oncologics are covered under the medical benefit provisions of healthcare plans and are a highly political class of drugs. Thus, we can determine if price plays a role in widely varying classes of drugs, or if the role of price varies by therapeutic class.

Initially, we used public sources to determine the price of our select drugs. The Red Book 2012 provides the list price of drugs by number of pills (e.g. a 30 pill container) and by bag size (e.g. a 15 ml bag or a 100 ml bag). Then, for each of the oncologics, we performed some additional calculations using the prescribing information for each drug to determine the approximate number of bags an average male would receive, thus controlling for different dosing. This was not necessary for the FDCs as each of these drugs are dosed at one pill per day independent of patient body mass. Next, we used Medicare's online Formulary Finder to determine the tier coverage of the select FDCs. We were unable to do this for the oncologics as they are predominantly covered under Part B, and thus, their coverage information is not publicly available. The Formulary Finder data showed that Caduet, the most expensive of the select FDCs, has the most restricted coverage of the three drugs suggesting that price may play a large role in the coverage decision-making process for these drugs.

To evaluate the role of price further, we interviewed five payers about their coverage decision-making process for our select FDCs and oncologics. Unanimously, all five payers said that pricing and contracting play a very important role in coverage decisions for FDCs. However, they said that coverage decisions for oncologics were more complicated and involved numerous

other factors besides price, and that price did not play as important of a role in coverage decisions.

Our hypothesis that the relatively high list prices of Caduet, Provenge, and Avastin would result in greater access restrictions and that price is the driving factor that has caused payers to provide relatively restricted coverage is partially correct. For Caduet, our results indicate that its relatively high list price is in fact the driving factor for its greater access restrictions compared to other cardiovascular FDCs. However, for Provenge and Avastin, not only is price not a driving factor in coverage decisions, but also these drugs do not have greater access restrictions in comparison to other oncologics. This is partially due to the reimbursement system for intravenous oncologics and partially because numerous other factors play a more important role in the decision-making process for oncologics.

### ***Impact of Price for Fixed Dose Combination Cardiovascular Drugs***

Our results imply that price plays a very important role in coverage decisions for fixed dose cardiovascular drugs. Our results also show that contracting is equally important in this class. All payers said that pricing and contracting go hand-in-hand for this class of drugs. Interestingly, the importance to payers of FDCs pricing and contracting poses a challenge for pharmaceutical companies with respect to optimizing their revenue potential.

In theory, pharmaceutical companies could maintain a high list price and then contract to a price which is lower than competitors. This would be one strategy for optimizing revenue since some payers may not need as steep of a contract as others to give the drug preferred access. However, this strategy is more difficult to manage as it requires the pharmaceutical company to negotiate a customized contract with every single payer rather than simply referring to the list price. The financial gains and losses for this strategy would have to be evaluated by each pharmaceutical company before deciding on an approach.

Payers mentioned other contracting strategies rather than simply a price rebate that are used by pharmaceutical companies in this class. One strategy is bundling. Bundling occurs when a

pharmaceutical company contracts for improved access of more than one drug at a time. For example, I will give you a 20% reduction in price if you put both Caduet and Lipitor on Tier 2. This allows large pharmaceutical companies to take advantage of their large portfolio of products.

Whether pharmaceutical companies should even contract at all for this class of drugs is questionable. Caduet appears to have very limited access – 80% of the plans we looked at through Formulary Finder did not cover Caduet at all, precluding members from any access. In this case, Pfizer, the manufacturer of Caduet, might consider contracting to be able to obtain a minimal form of access. However, when we spoke with payers, most of them indicated that Caduet's price would have to be severely reduced. On the other hand, Vytorin does not have as good access as Exforge, but it is on the formulary for most of the payers. Merck would have to analyze whether lowering Vytorin's price to obtain better access would result in enough increased sales to compensate for the price reduction. The reduction in price may not be worth the extra utilization.

In general, the payers we spoke with did not view fixed dose combination drugs positively. One payer does not cover any of the FDCs because their company does not see any added value in them. They do not believe in the compliance argument, and believe that FDCs are often contrived and merely life-style drugs. Another issue that payers have with FDCs is that they potentially expand the patient pool without an additional copayment in that patients who would normally be on just one of the drugs in the FDC end up taking both. One payer mentioned that to obtain better coverage for an FDC, the pharmaceutical company would have to lower its price below that of the two individual components to incorporate the loss of the copayment. Finally, payers understood that FDCs are generally a strategy to increase a drug's patent life and maintain a relatively high price point. Thus, while the payers we spoke with tended to discourage use of the cardiovascular FDCs for cost reasons, they had other grounds for concern as well.

The fixed dose combination cardiovascular drugs were intended to model a therapeutic area where the products are considered to have minimal advantages over competitors and generics are available. Extrapolating from our results would imply that in other therapeutic areas, such as

diuretics and asthma drugs, where generics are available and where there are minimal perceived advantages between products, pricing and contracting play strong roles in the determination of coverage of the products. Payers' generally negative attitude toward FDCs would likely come into play as well. This should be confirmed with further studies.

### ***Impact of Price for Intravenous Oncologics***

Contrary to our hypothesis, our results show that price plays a very limited role in coverage decisions for intravenous oncologics. The only impact that payers stated price played for these drugs was in determining which drugs should be subject to prior authorization. Payers place prior authorizations on the drugs with the highest price to make sure the product is being used for an appropriate use, since overall cost to the company is impacted by the combination of price and utilization, including off-label use.

Interestingly, although payers ranked efficacy for intravenous oncologics very high, they stated that better or worse efficacy would not impact the coverage of these drugs as long as the drug is FDA approved. For some of these drugs, payers do require patients to take the accompanying diagnostic to show that the drug will most likely be effective (e.g. Vectibix and Erbitux). But their coverage of intravenous oncologics does not strongly depend on how effective the drug is as long as it is FDA approved.

In general, payers stated two reasons why price and efficacy do not play a significant role in reimbursement decisions for these drugs. First, there are many other factors, such as public policies and unmet need, which come into play for this class of drugs. Second, payers lack the tools and ability to guide members to other treatments for this class of drugs because they are covered under the medical benefit / Part B.

Many states have mandates to cover all FDA approved indications for oncologics. Some states such as Connecticut even mandate that payers cover all off-label use of oncology drugs.<sup>30</sup> This prevents payers from simply not covering a drug due to efficacy or safety concerns. Additionally, this prevents payers from dissuading drug companies from pricing high because payers are

precluded from not covering the drug or putting significant access restrictions on it. Several states, such as New York, Vermont, and Maine, are passing laws which put limits on the co-payments and co-insurance amounts payers and healthcare plans can place on drugs. The goals of these laws are to protect patients from very high out-of-pocket costs. Interestingly, pharmaceutical companies such as Pfizer are avidly supporting these laws. They are even offering to draft the legislative language. According to Sharon Treat, executive director of the National Legislative Association on Prescription Drug Prices, these laws give “the drug companies a free ride to charge as much as they want.”<sup>31</sup> Currently, high out-of-pocket costs is the only tool that payers have to dissuade drug companies from pricing their oncology drugs high. The out-of-pocket cost is meant to dissuade members from using the drugs unnecessarily, and thus, would lower the drug’s overall utilization and the revenue for the pharmaceutical companies. Although these new laws protect patients from significant out-of-pocket costs, they eliminate the one tool payers can use to dissuade pharmaceutical companies from pricing their oncology drugs so relatively high. Oncology being one of Medicare’s six protected classes has a similar effect.

Payers have difficulty managing drugs covered under the medical benefit / Part B due to the structure of the healthcare system. Unlike the pharmacy benefit, there are no out-of-pocket tiers for medical benefit drugs, nor step edits because the medical benefit drugs are not distributed at retail pharmacies. The only tools that payers have are prior authorizations and co-insurance. Prior authorizations are difficult for payers to enforce due to the structure of the system. Thus, payers have no method to give more efficacious drugs preferred access. Under the current system, physicians first purchase the drug from a distributor, then give the drug to the patient, and then finally bill the patient’s insurance company. By the time the physician bills the insurance company, he/she has already given the patient the drug, making it difficult for payers to deny reimbursement for that drug. As a result, prior authorizations are difficult to enforce and require payers to make sure their in-network physicians are well versed in the prior authorization requirements for every drug.

The out-of-pocket amount for drugs with a co-insurance does vary with the price of the drug. The higher the list price of the drug, the larger the out-of-pocket cost. However, since almost all

plans have an annual out-of-pocket limit, members taking oncologics usually reach this limit within the first few months of treatment. Once a member reaches their out-of-pocket limit, the effects of having a co-insurance on a drug is negated. Additionally, as mentioned earlier, many states are passing laws that limit payers' abilities to place co-insurances on these drugs. Thus, with the current structure of the healthcare system, payers have minimal ability to curb drug costs for intravenous oncologics. By inference, this is true for all drugs covered under the medical benefit.

The structure of the medical benefit / Part B also prevents payers from giving preferential access to drugs with better efficacy because all of the drugs have the same co-insurance level. Thus, an intravenous drug with improved efficacy would have the same level of coverage as a less-effective drug. This structure leaves the differentiation of efficacy predominantly up to the physician. With this structure, physicians and patients are not incentivized to use one drug over the other as they are with drugs covered under the pharmacy benefit / Part D. However, there are oncology distributors that use efficacy to determine access to a drug. The oncology distributor we spoke with indicated that the first determinant of whether a drug will be included in their treatment guidelines was efficacy. If the drug showed improved efficacy, then it would be the recommended product regardless of price and other factors.

### ***Evolving Landscape of Drug Management***

Although we did not focus on new techniques payers are using to attempt to control rising drug costs, payers mentioned several of them during our interviews. Two of the emerging strategies to control costs are the use of specialty pharmacies and the role of certain oncologic drug distributors. In some cases payers are collaborating with the specialty pharmacies and distributors to control costs. In other cases, the specialty pharmacies and distributors are working independently.

Specialty pharmacies are organizations that provide access to, and support for, most out-patient intravenous and injectable products that have relatively high acquisition costs and are difficult to manage. Specialty pharmacies act as an intermediary between physicians and payers for these



products. They handle the inventory and sourcing of the drugs for the physicians so that physicians no longer have to worry about stocking the intravenous and injectable drugs themselves. By billing the payer for reimbursement on behalf of the physician, the specialty pharmacies also take care of making sure that all prior authorizations issued by payers are followed before the drug is given to the physician.<sup>36</sup> Some payers are considering mandating that physicians obtain their oncologies via their specialty pharmacy. WellPoint, for example, has its own in-house specialty pharmacy. WellPoint's chief pharmacy officer, Brian Sweet, has stated that their goal with their specialty pharmacy is to be able to utilize "the same formulary management and utilization management techniques that we've done in pharmacy, and putting them in the medical benefit."<sup>21</sup> The increased use of specialty pharmacies by payers will increase their ability to manage drugs covered under the medical benefit.

US Oncology is an oncology drug distributor to physicians. The company also manages over 1,200 physicians' back office needs such as billing and electronic health records. In collaboration with their physicians, US Oncology has developed "Level I Pathways" for treating non-small cell lung cancer and colorectal cancer. The goal of the program is to steer physicians to treatment options that provide maximal survival benefit, minimal toxicities, and cost-savings opportunities. They have conducted studies with non-small cell lung cancer and colorectal cancer patients demonstrating that their "Level I Pathways" result in no decrease in overall survival, but a significant decrease in the overall cost of care. As a result, the "Level I Pathways" guidelines have been adopted by over 80% of physician practices in US Oncology's network.<sup>37, 38</sup> This is an example of how a drug distributor is playing a role in curtailing drug costs. US Oncology is not owned by a payer. However, US Oncology is a unique organization in that it is both a drug distributor and physician office manager. Most drug distributors do not manage their physician's electronic health records systems. Although there are few other companies with a similar business model to US Oncology, this is a possible mechanism that payers or other third party organizations could use to control the cost of intravenous oncologies.

Outside of the United States, different methods are used to control costs. The United Kingdom uses the National Institute for Health and Clinical Excellence (NICE) to determine which drugs should be covered by its National Health Services (NHS). For new drugs, NICE develops and

publishes clinical guidelines, which incorporate both efficacy and cost. NICE uses quality-adjusted life years (QALYs) to measure the health benefits delivered by a given treatment regime. As a guideline, NICE accepts as cost effective those interventions with an incremental cost-effectiveness ratio of less than £20,000 per QALY. NICE requires increasingly strong reasons for accepting as cost effective interventions with an incremental cost-effectiveness ratio over a threshold of £30,000 per QALY.<sup>32</sup> Both Avastin and Vectibix did not meet NICE's cost-effectiveness threshold and thus, are not covered by NHS.<sup>33</sup> Germany has sickness funds which act as budgets from which physicians draw to treat patients. All German citizens with incomes below roughly \$60,000 are required to enroll in one of approximately 250 sickness funds. Those with higher incomes may enroll in the funds if they wish, or may opt out of the government system. The costs of drugs are paid by the sickness funds. Thus, the physician is dissuaded from prescribing costly products as they are on a fixed budget.<sup>34</sup> Finally, in France new drugs are assigned an ASMR rating of I to V based entirely on efficacy data, where an ASMR rating of I represents a major improvement over existing therapies and an ASMR rating of V represents no improvement over existing therapies. Based on the ASMR rating, a price is negotiated with the pharmaceutical manufacturers. Sometimes price/volume agreements are put in place, where if the drug exceeds a certain volume of use, rebates kick-in and the drug company is forced to lower its price.<sup>35</sup> These are simply a few examples of how other countries are attempting to control increasing drug prices.

### ***Future Research***

Our discussions with payers and our analysis of the pricing and reimbursement issues involved with FDC cardiovascular drugs and intravenous oncologics offer significant implications for future research. This study looked at the issues of pricing and reimbursement from a qualitative, broad perspective, given there has been little research previously conducted surrounding reimbursement decisions and the variances in coverage decision-making processes. There are numerous preliminary learnings from this study which should be explored further.

Increasing the number of payers interviewed to expand the sample size to the level of mathematical significance would be beneficial. Although this study was able to reach just under

50 million covered pharmacy/Part D lives and just fewer than 100 million covered medical/Part B lives, the support of the findings would be increased by interviewing additional payers. This would also allow for analysis of regional differences in the decision-making process. This study has shown that coverage of oncologics is strongly impacted by the presence of state mandates for coverage of these drugs. Understanding which regions have a strong local impact on coverage decisions would be beneficial.

This study began to explore the role of other healthcare organizations outside of payers in deterring pharmaceutical companies from pricing their products too high. There have been very few studies conducted on the role of drug distributors regarding drug access. Interviewing additional drug distributors and analyzing how they are managing their oncology pricing would be worthwhile. Understanding if other oncologic distributors have the infrastructure in place to manage oncologic usage and if their decision-making process regarding drug coverage differs from that of payers are important factors to understand. We briefly touched on the emerging role of in-house specialty pharmacies. However, we did not explore the impact of independent specialty pharmacies, and their impact on patient access to drugs and what role pricing plays in their decision-making process. Are there other organizations attempting to control drug spending?

Finally, a key opportunity to further validate the implications suggested by this thesis would involve exploring the rationale behind the coverage decision-making process for drugs in other therapeutic areas. Some possible therapy areas are diabetes and asthma drugs, as each of these have both branded and generic drugs with comparable efficacy. Other interesting therapy areas may be anti-psychotics and anti-epileptic drugs, since these classes of drugs are each one of Medicare's six protected classes, but the products are covered under the pharmacy benefit. Lastly, this thesis did not explore the management of drugs predominantly administered within a hospital such as branded anti-biotics.

## Chapter 6: Conclusions

Our results show that price plays an important role in the coverage decision-making process only for certain therapeutic classes. The two therapeutic areas chosen had widely different roles for price in the decision-making process. Other factors also played different roles in the coverage decision-making process for these two classes. Additionally, our research highlighted the stark difference in payers' abilities to manage drugs covered under the pharmacy benefit / Part D versus those covered under the medical benefit / Part B. Specifically, the ability to manage drugs under the medical benefit / Part B is significantly less than the ability to manage drugs under the pharmacy benefit / Part D. This difference diminishes the impact that price and efficacy have over the coverage of intravenous drugs, since payers are severely limited in their ability to grant more efficacious or less expensive drugs preferential access if they are covered under the medical benefit / Part B. However, there are emerging organizations and techniques that may change payers' ability to manage these drugs as well as change the role of price with respect to patient access to medical benefit / Part B drugs. Thus, our research has several implications for the management of pharmaceuticals and the role of price in their management.

### *Implications*

- 1) List price and contracting play an important role in classes of drugs which are covered under the pharmacy benefit / Part D, and where there are minimal perceived advantages between the drugs.
- 2) List price and contracting play less important roles for classes of drugs covered under the medical benefit / Part B.
- 3) Improved efficacy for intravenous drugs covered under the medical benefit / Part B does not correlate with improved access because payers are unable to differentiate access to the medical benefit / Part B drugs.
- 4) Public policy and unmet need are important factors driving coverage decisions for oncology drugs.
- 5) Currently, payers have minimal to no tools available for them to manage drugs covered under the medical benefit / Part B.

- 6) Pharmaceutical companies support public policies mandating coverage of classes of drugs or limiting the out-of-pocket costs because it allows them to price these drugs without having to factor in payers possibly not covering the drug or passing on a significant part of the drug's cost to the patient.
- 7) Drugs entering therapeutic areas with no other treatment options have greater pricing liberties.
- 8) Although the coverage decision-making process is similar across payers, the specific weighting of the various factors that go into the process may vary.
- 9) Regional differences can have an impact on the coverage decision-making process for some therapeutic areas.

## **Appendix A: Medicare Formularies Represented**

### ***National Plans***

- United Healthcare
- Aetna
- Health Net
- CIGNA
- Humana
- WellCare
- WellPoint

### ***Regional Plans***

- Blue Shield of California
- Blue Cross Blue Shield of Texas
- Blue Cross Blue Shield of Illinois
- Blue Cross Blue Shield of New Mexico
- Blue Cross Blue Shield of Oklahoma
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